21 can be found in original claims 1-4; on page 6, lines 16-20 and page 43, line 23 to page 44, line 6 wherein administration to humans is discussed. Respectfully, a person skilled in the art would understand the phrases "pharmaceutically acceptable carrier" and "pharmaceutical composition" to be suitable for administration to human beings.

Written description support for the amendment to claim 28 can be found in original claim 14 and on page 6, lines 11-15. Support for new independent claim 36 is found at page 6, lines 16-20 and in original claim 14 ("cytotoxic moiety"). Similarly, support for new independent claim 38 is found at page 13, lines 16-18 and in original claim 14. New dependent claims 37 and 39 are supported by original claims 14-15.

I. Summary of the Office Action

1. The request for a continued prosecution application based on parent application 08/980,395 was established. All outstanding rejections in the parent application were withdrawn in favor of the rejections set forth below.

2. Claims 28 & 32-35 were rejected under 35 U.S.C. § 112, first paragraph for containing new matter because their is no basis in the specification for chlorotoxin fused to any protein.

3. Claims 30-31 were rejected under 35 U.S.C. § 101 (statutory-type double patenting) as claiming the same invention as that of claims 1 & 3 of U.S. patent 6,028,174.

4. Claim 28 was rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. patent 6,028,174.

5. Claims 21-23 were rejected under 35 U.S.C. § 102(b) as being anticipated by DeBin *et al.* (1993) Am. J. Physiol. 264, C361-369.

6. Claims 21-23 were rejected under 35 U.S.C. § 102(b) as being anticipated by Hall *et al.* (1993) U.S. Patent 5,223,253.

7. Claims 21-35 were rejected under 35 U.S.C. § 103(a) as being unpatentable over DeBin *et al.* (1993) in view of Hammock *et al.* (1998) U.S. Patent 5,756,340 and Phillips *et al.* (1994) Cancer Res. 54, 1008-1015.

G

II. Response to the Office Action

In the telephonic interview on April 12, 2001 and as set forth in the summary of the telephonic interview issued by the Examiner (Paper No. 27), the Examiner agreed to withdraw the statutory-type double patenting rejection of claims 30-31 in response to Applicants' arguments. In response to the obvious-type double patenting rejection of claim 28, Applicants agreed to submit a terminal disclaimer to overcome the rejection. Applicants respectfully request that this latter rejection be held in abeyance until such time that allowable subject matter is found with the understanding that a disclaimer will be provided at that time.

Claims 28 & 32-35 were rejected under 35 U.S.C. § 112, first paragraph for containing new matter because their is no basis in the specification for chlorotoxin fused to any protein. In the telephone interview, the Examiner agreed to withdraw this rejection if the term "chlorotoxin fusion protein" was incorporated into the claim language. Applicants have amended claim 28 as suggested by the Examiner and therefore respectfully request that the rejection be withdrawn.

III. Rejections based on 35 U.S.C. § 102

Claims 21-23 were rejected under 35 U.S.C. § 102(b) for purportedly being anticipated by DeBin *et al.* Applicants have amended claim 21 to provide the feature that the pharmaceutical composition be "suitable for use in humans" which is not disclosed by the cited reference. Applicants acknowledge that this reference does disclose a preparation containing chlorotoxin that is administered to various animal species (*i.e.*, two arthropods – crayfish and cockroaches). In fact, the composition is administered in order and in a dosage range sufficient to paralyze or kill these arthropods. However, neither administration of such compositions to humans nor the treatment of glial-derived tumor cells simply are not contemplated by this reference.

Thus, applicants submit that amended claim 21 and its dependent claims are not anticipated by DeBin *et al.* because this reference does not disclose a pharmaceutical composition suitable for use in humans. The purified chlorotoxin produced by DeBin *et al.* was reconstituted in 10 mM trifluoroacetic acid (see page 363, column 2, fifth paragraph) prior to dilution in water to a final volume of only 10 1 (see page 363, column 2, third paragraph).

Respectfully, a composition processed with such a high concentration of trifluoroacetic acid as in the DeBin *et al.* reference does not appear to be a suitable pharmaceutical composition for use in humans and does not anticipate the pending claims. Moreover, as discussed in the Rule 132 Declaration of Dr. Howard L. Levine, accompanying the response filed by Applicants on February 5, 2001, the DeBin preparation, in addition to containing TFA, was also contaminated by other venom constituents and was not even reconstituted in sterile water. Where the reference mentions reconstituting various preparations in water, it explicitly mentions deionized water but does not mention sterile water, which would be found in compositions suitable for administration to human patients.

Applicants also bring to the attention of the Examiner the Blake *et al.* (1969) (Toxicol. Appl. Pharmacol. 15, 83-91) which assessed the toxic effects of trifluoroacetic acid administration in mice. In the abstract of this peer-reviewed journal publication, the authors state that "free trifluoracetic acid was as toxic as hydrochloric acid" (see page 83, abstract, lines 17-18). Blake *et al.* further state that administration of 150 mg/kg trifluoroacetic acid resulted in death in two of five animals and that hydrochloric acid produced the same effect at an equivalent dose (see page 88, lines 1-3). Applicants respectfully submit that trifluoracetic acid is certainly not suitable for administration in humans.

Claims 21-22 also were rejected under 35 U.S.C. § 102(b) for purportedly being anticipated by Hall *et al.* In light of the amendment to claim 21 requiring the composition to be suitable for use in humans, Applicants submit that the cited reference is no longer applicable because it discloses a chlorotoxin composition for use as a bovine adjuvant. Applicants bring to the Examiner's attention the abstract of the cited reference which discloses a vaccine composition comprising inactivated bovine Trichomonas cells in combination with an effective amount of suitable adjuvant. Applicants submit that the chlorotoxin (adjuvant) in combination with the Trichomonas cells does not constitute a pharmaceutical composition suitable for use in humans and therefore does not anticipate the pending claims.

IV. Rejections based on 35 U.S.C. § 103

Claims 21-35 were rejected under 35 U.S.C. § 103(a) as being unpatentable over DeBin

9

et al. in view of Hammock *et al.* and Phillips *et al.* Applicants respectfully submit that DeBin *et al.* does not teach nor suggest all of the limitations of the claims for the reasons discussed above. In the absence of DeBin *et al.*, Applicants submit that the remaining references do not render claims 21-35 obvious. The Office Action has relied upon the cited references for their purported disclosure of a pharmaceutical composition comprising chlorotoxin. Applicants submit that the combination of such elements fails to meet the claim limitation providing for a pharmaceutical composition suitable for use in humans. Applicants respectfully request that the rejection be withdrawn.

IV. Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted
Morgan, Lewis & Bockius LLP

Dated: **July 30, 2001**
Morgan, Lewis & Bockius LLP
Customer No. **09629**
1800 M Street, N.W.
Washington, D.C. 20036
202-467-7000

Michael S. Tuscan
Registration No. **43,210**

6

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 21 has been amended as follows:

21. (Once Amended) A pharmaceutical composition comprising chlorotoxin [~~and a pharmaceutically acceptable carrier~~] wherein the pharmaceutical composition is suitable for use in humans.

Claim 28 has been amended as follows:

28. (Once Amended) A pharmaceutical composition comprising a chlorotoxin [~~fused to a second~~] fusion protein [~~and a pharmaceutically acceptable carrier~~].

Claim 29 has been amended as follows:

29. (Once Amended) The composition of claim 28 wherein the [~~second~~] chlorotoxin fusion protein [~~is~~] comprises chlorotoxin fused to glutathione-S-transferase.

Claim 30 has been amended as follows:

30. (Once Amended) The composition of claim 28 wherein the [~~second~~] chlorotoxin fusion protein [~~is~~] comprises chlorotoxin fused to a cytotoxic agent.

Claim 32 has been amended as follows:

32. (Once Amended) The composition of claim 28 wherein the [~~second~~] chlorotoxin fusion protein is labeled.

G